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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/521,066      | 10/11/2005  | John V. Frangioni    | BIDM-P01-014        | 6848             |

28120 7590 04/06/2007  
FISH & NEAVE IP GROUP  
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BOSTON, MA 02110-2624

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| EXAMINER |
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AUDET, MAURY A

|          |              |
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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1654

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE  | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS                               | 04/06/2007 | PAPER         |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/521,066

Applicant(s)

FRANGIONI, JOHN V.

Examiner

Maury Audet

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/05/02/06</u>   | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

Claims 1-34 are pending and examined on the merits. The present application contains priority back to PCT/US03/21478, for which an International Search Report over nearly identical claims has already been conducted (Examiner Brumback). At it's narrowest reagent (claim 11) out of respective genres for a conjugate between an infrared fluorescent substance and a targeting moiety, the reagent is a quantum dot conjugated to annexin V.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Packard et al. (US 2003/0211548) in view of Licha et al. (US 2001/00055567 A1, cited in the International Search Report).

Packard et al. teach a reagent comprising annexin V-conjugated to examples of fluorescent labels for use in a pharmaceutical preparation for imaging cell death/apoptosis (e.g. para 77, 15, 126-127, claims 91-92, entire document). Packard et al. also teach quantum dots useful as highly fluorescent labels (e.g. para 82). However, Packard et al. does not expressly teach the conjugation of the annexin V-conjugate (conjugated to examples of fluorescent labels) to the quantum dots recited as known fluorescent labels.

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Licha et al., discussed in the International Search Report, teaches the present claims 1-6 and 12-34, and renders obvious claims 7-9, especially the near-infrared fluorescent dye genus of present claim 2 (entire document, esp. Examples 1-3). Licha et al. was not deemed to teach annexin V-conjugated to examples of fluorescent labels for use in a pharmaceutical preparation for imaging cell death/apoptosis or quantum dots useful as highly fluorescent labels (e.g. Applicant's claims 10-11).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to conjugate the annexin V- conjugate to any fluorescent dye such as near-infrared fluorescent dyes or quantum dots for the imaging of apoptosis/cell death in Packard et al., because Licha et al. advantageously teach that annexin's may be conjugated to near-infrared fluorescent dyes for the same purpose and Packard et al. advantageously teach that specifically annexin V is conjugated to fluorescent agents, followed by a description that quantum dots are also known for use as fluorescent agents. Based on these teachings on of ordinary skill in the art would have been motivated to conjugated any annexin, including annexin V, to the near-infrared fluorescent dyes of Licha et al. or the quantum dots recited in Packard et al., for the purpose of imaging apoptosis, based on the advantageous teachings of the references to this combination using annex/annexin V and the desired effects/availability of the recited options such as quantum dots.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

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the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***Conclusion***

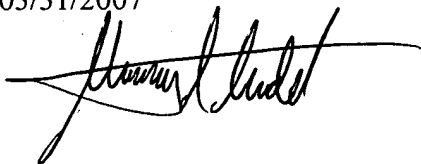
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 03/31/2007

A handwritten signature in black ink, appearing to read 'Maury Audet', with a long horizontal stroke extending to the left.

MAURY AUDET  
PATENT EXAMINER